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# Density mediated drug release from dapivirine vaginal rings produced by additive manufacturing

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## Key points

1

DDM printing on an Arburg Freeformer has been shown to create vaginal rings with a range of densities.

2

DDM printing on an Arburg Freeformer has provided a new potential to either increase the release rate of poorly water soluble compounds or reduce the loading required to maintain a desired release rate.

3

VRs with an infill density of 100% manufactured by IM and DDM released up to 4 and 10% of their total DPV loading, while rings with an infill density of 50 or 10% (DDM) released up to 56 and 79% of their total DPV loading after 29 days.

## Background

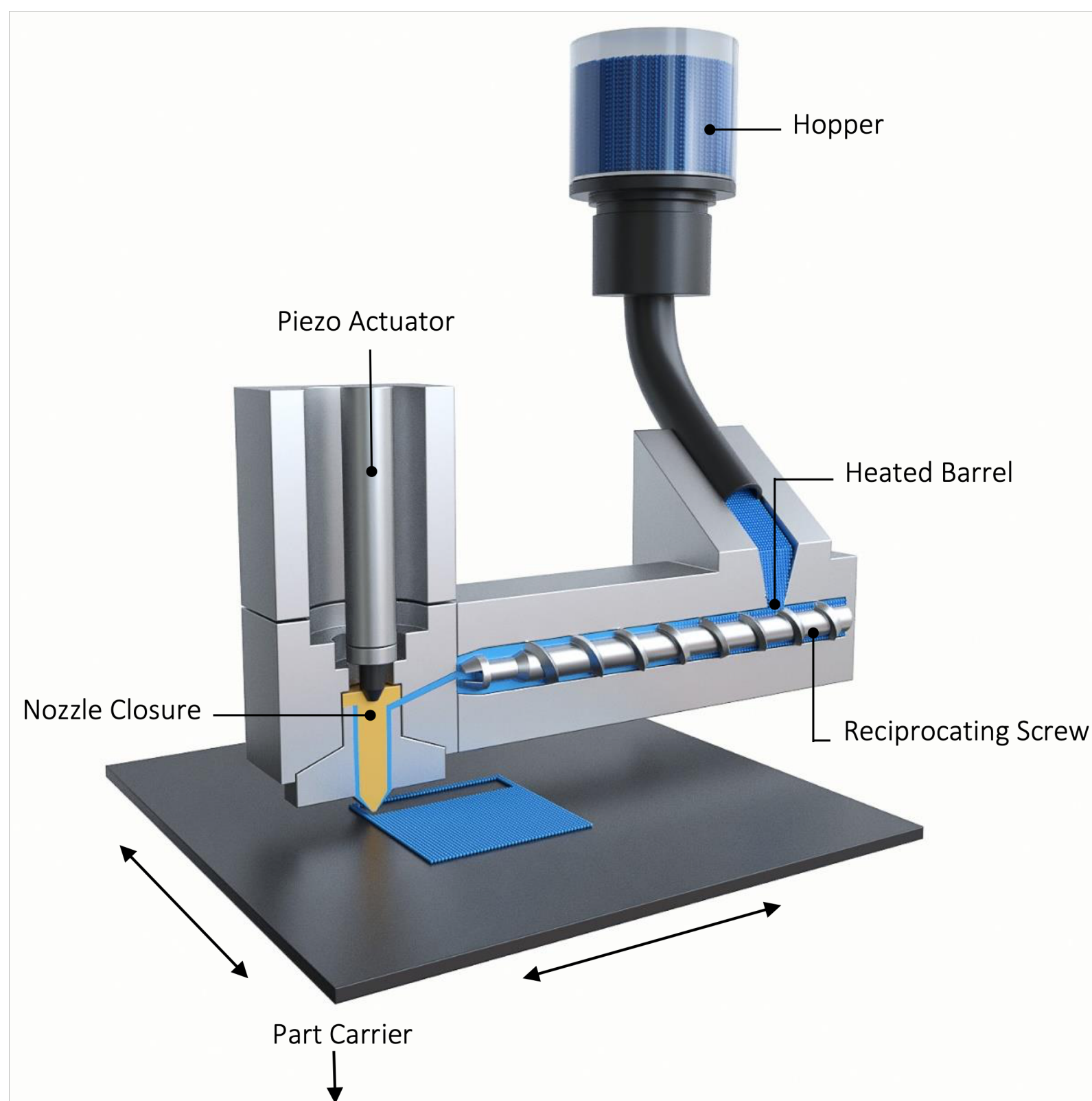
Droplet deposition modelling (DDM) is a form of 3D printing that fuses droplets of molten polymer to create each layer, providing exquisite levels of control over an object's design and morphology. Such manipulation allows properties including density, geometry and surface area to be manipulated in ways that have been unthinkable using conventional thermoplastic processing techniques. Here we utilise the DDM process and compare this to injection moulding (IM) to produce dapivirine (DPV) loaded vaginal rings using a pharmaceutically relevant, life science grade thermoplastic polyurethane.

## Objectives

Identify grades of TPU which are compatible with both additive manufacturing (DDM) and traditional manufacturing processes (IM).  
• Thermoplastic polymers should have  $\leq 2\%$  weight loss at processing temperature as assessed by TGA.  
Compound filament with 10% w/w DPV and pelletise to produce pellets  $\sim 2.0$  mm.  
Compare drug delivery and other physiochemical properties of vaginal drug delivery devices fabricated by additive manufacturing (DDM) against conventional manufacturing techniques (IM).

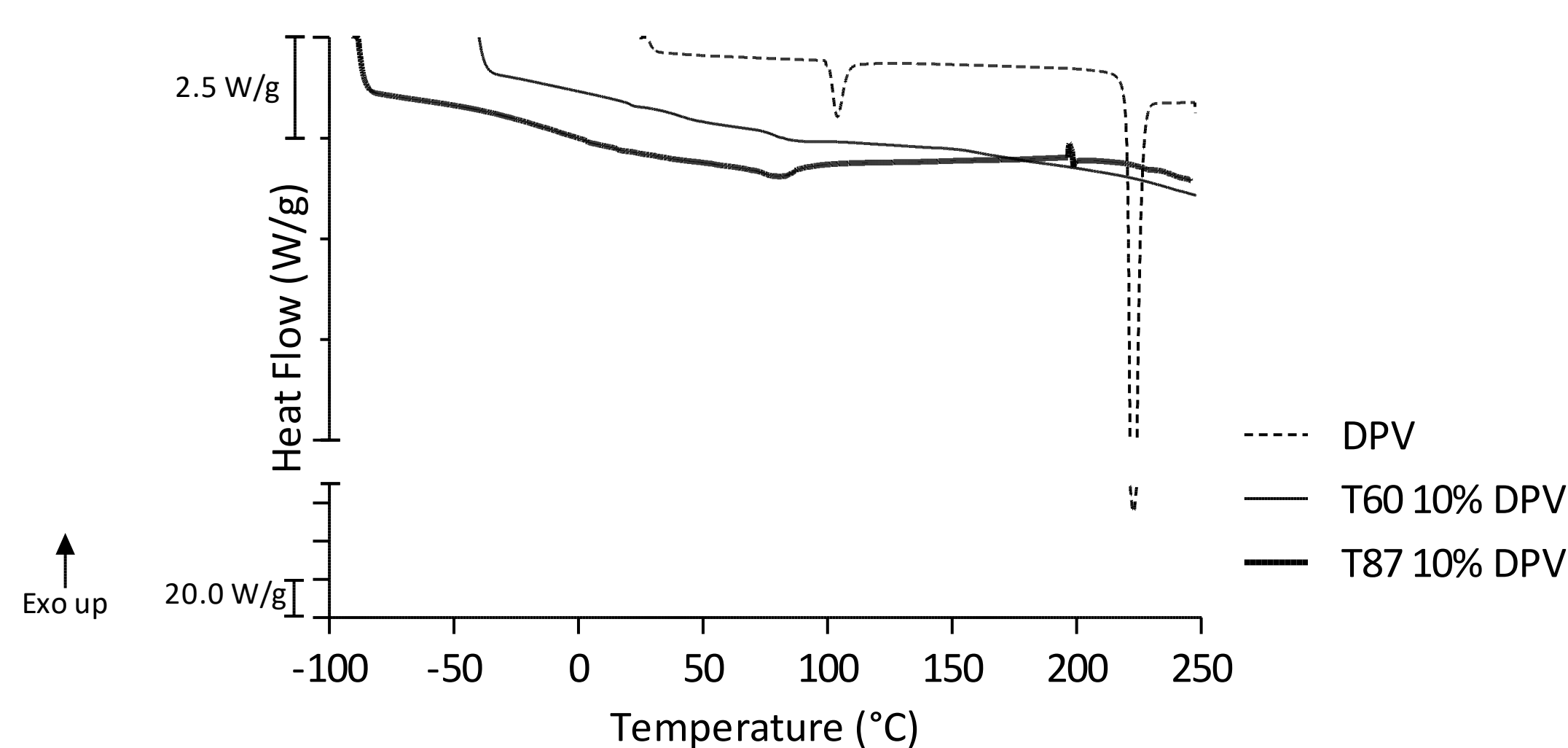
## Methods

Vaginal rings (54.0 mm outer diameter, 4.0 mm cross sectional diameter) were fabricated by injection molding or Arburg Plastic Freeforming – a proprietary DDM process, using a hydrophobic TPU (T87 or T60) loaded with 10% w/w dapivirine. Using the DDM process, rings of 100, 50 and 10% matrix density were produced. Rings were evaluated for in vitro drug release over 29 days in an aqueous release media and assessed for thermal characteristics.

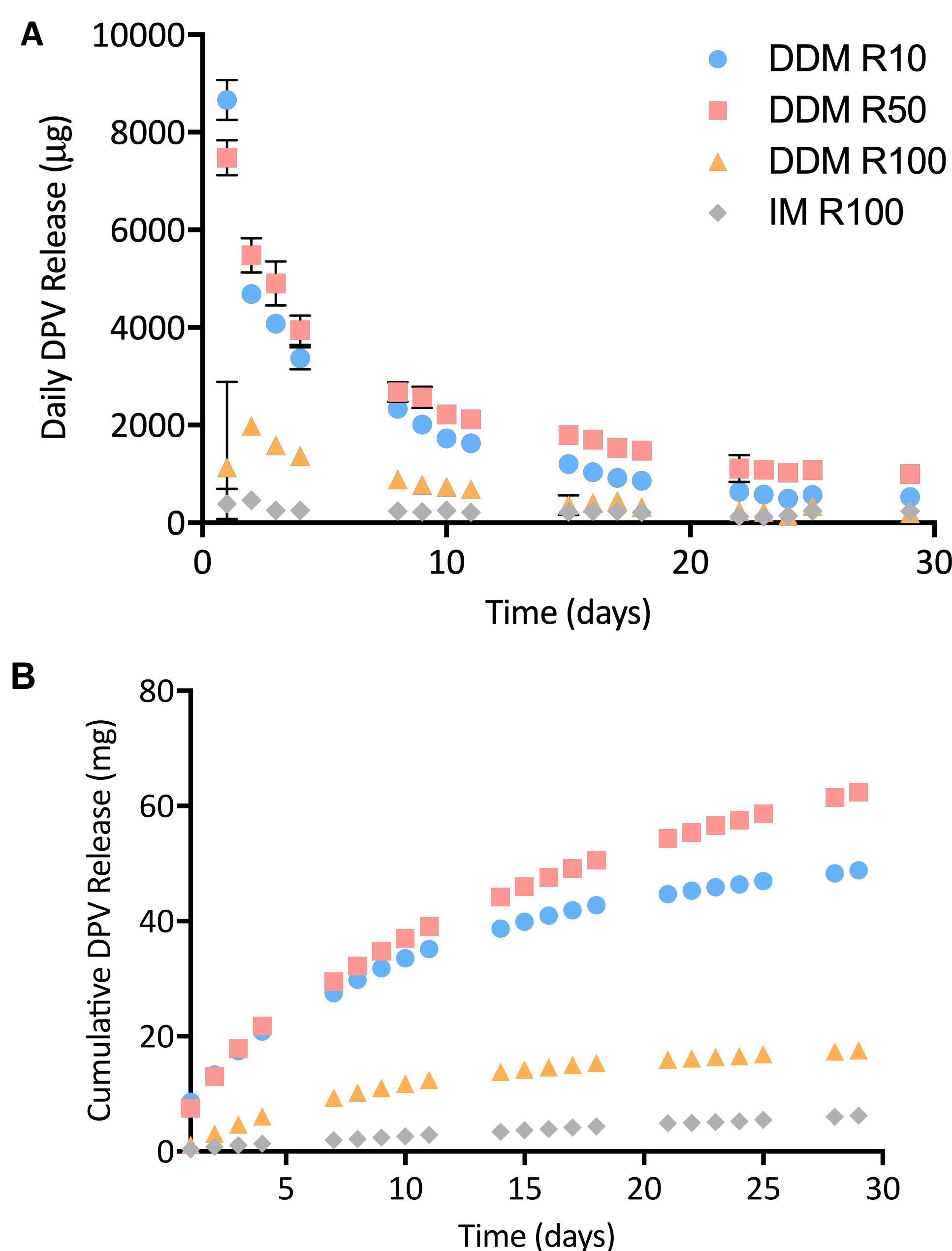


**Fig. 1:** Diagram of Arburg Freeformer and internal components.

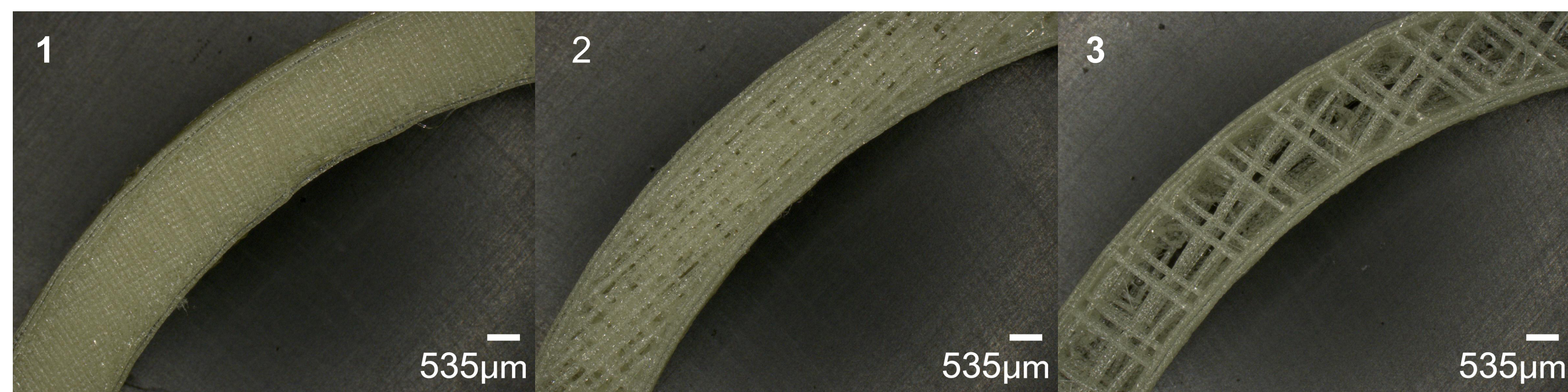
## Results



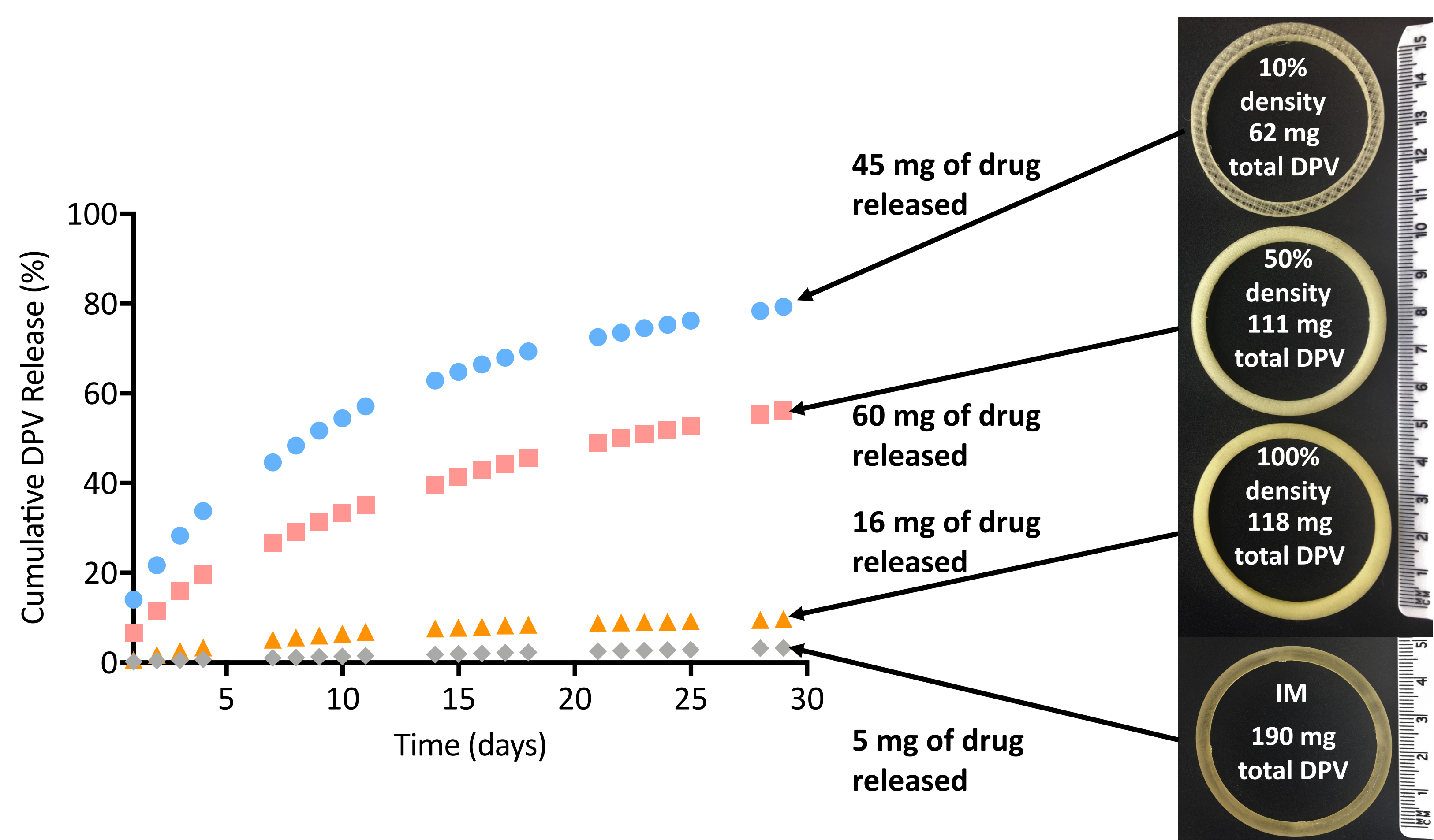
**Fig. 2:** DSC thermal trace for model drug (DPV), DPV loaded (10% w/w) T87 and T60 filament (n=3, representative data shown). Samples were heated from either  $-90^{\circ}\text{C}$  or  $-50^{\circ}\text{C}$  to  $250^{\circ}\text{C}$  at a rate of  $20^{\circ}\text{C min}^{-1}$ .



**Fig. 3:** (A) Daily (Mean  $\pm$  SD, n=6) and (B) Cumulative release (n=6) of DPV from T87-DPV vaginal rings (outer diameter 54.00 mm, cross-sectional diameter 4.00 mm, fabricated by injection molding (IM) or droplet deposition modelling (DDM) with densities of 10% (R10), 50% (R50) or 100% (R100). In-vitro release was performed in a 0.2% tween solution.



**Fig. 4:** Digital images showing the base of a quarter of T87-DPV VRs (outer diameter 54.00 mm, cross-sectional diameter 4.00 mm) fabricated by droplet deposition modelling with an infill density of (1) 100%, (2) 50% and (3) 10%.



**Fig. 5:** Cumulative release plotted as a percentage of the total drug loading in each of the vaginal ring types (n=6) of DPV from T87-DPV vaginal rings (outer diameter 54.00 mm, cross-sectional diameter 4.00 mm, fabricated by injection molding (IM) or droplet deposition modelling (DDM) with densities of 10%, 50% or 100%. In-vitro release was performed in a 0.2% tween solution. The ring photographs indicate the density and total drug loading (mg) for each type of ring.

**Table 1:** Dimensional analysis of DDM printed VRs (n=6) manufactured using T87-DPV or T60- DPV

Sample (n=6)	Mass (g)	Cross-sectional Diameter (mm)	Outer Diameter (mm)
T87-DPV R10	$0.62 \pm 0.02$	$4.12 \pm 0.25$	$53.62 \pm 1.11$
T87-DPV R50	$1.11 \pm 0.03$	$3.99 \pm 0.07$	$53.70 \pm 0.49$
T87-DPV R100	$1.81 \pm 0.04$	$4.00 \pm 0.06$	$53.57 \pm 0.34$
T60-DPV R10	$0.56 \pm 0.03$	$4.02 \pm 0.06$	$53.40 \pm 0.21$
T60-DPV R50	$1.09 \pm 0.03$	$4.00 \pm 0.05$	$53.59 \pm 0.20$
T60-DPV R100	$2.03 \pm 0.03$	$3.99 \pm 0.03$	$53.57 \pm 0.19$